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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/040,547	01/04/2002	Christine H. Blood	70025-04-CIP	3786

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EXAMINER	
KAM, CHIH MIN	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 09/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/040,547	BLOOD ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

P riod for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 8-27 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 8-27 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4/4/02 . 11/04/02 5/4/03
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

1. In the preliminary amendment filed June 18, 2002, claims 1-7 have been cancelled, thus claims 8-27 are examined.

2. Applicants indicate the middle initial of Inventor, Guy W. Herbert was misspelled as "H" in the original oath, a Petition to correct the spelling of the correctly named inventor has been filed May 10, 2002 and will be forward to Petition Office.

3. Some references listed in the Information Disclosure Statement filed April 4, 2002 are not considered because these references are not in the file and cannot be obtained by the Examiner. Please resubmit these references if applicants want them to be considered.

Claim Rejections-Statutory Basis Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

4. Claim 11 is rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 7 of prior U.S. Patent No. 6,579,968 because both sets of claims are directed to a pharmaceutical composition comprising a peptide of Ac-Nle-cyclo(-Asp-His-D-Phe-Arg-Trp-Lys)-OH and have identical scope. This is a double patenting rejection.

Claim Rejections-Obviousness Type Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or

improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 8-10 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of U. S. Patent 6,579,968. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 8-10 in the instant application disclose a pharmaceutical composition comprising a peptide and a pharmaceutically acceptable carrier, wherein the peptide is a free acid or pharmaceutically acceptable salt thereof comprising a sequence selected from the group consisting of His-Phe-Arg-Trp (SEQ ID NO:1), His-D-Phe-Arg-Trp, homologs of His-Phe-Arg-Trp and homologs of His-D-Phe-Arg-Trp. This is obvious in view of claims 1-7 in the patent which disclose a peptide of Ac-Nle-cyclo(-Asp-His-D-Phe-Arg-Trp-Lys)-OH or its pharmaceutically acceptable salt, or, a composition or a pharmaceutical composition comprising the peptide of Ac-Nle-cyclo(-Asp-His-D-Phe-Arg-Trp-Lys)-OH or its pharmaceutically acceptable salt. Both sets of claims cite a pharmaceutical composition comprising a peptide which is an acid and comprising His-D-Phe-Arg-Trp such as Ac-Nle-cyclo(-Asp-His-D-Phe-Arg-Trp-Lys)-OH or its pharmaceutically acceptable salt. Thus, claims 8-10 in present application and claims 1-7 in the patent are obvious variations of a pharmaceutical composition

comprising a peptide of Ac-Nle-cyclo(-Asp-His-D-Phe-Arg-Trp-Lys)-OH or its pharmaceutically acceptable salt.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 8-10, 20-22 and 24-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a pharmaceutical composition a pharmaceutical composition comprising the peptide of Ac-Nle-cyclo(-Asp-His-D-Phe-Arg-Trp-Lys)-OH (compound 1) or its pharmaceutically acceptable salt, a method of stimulating sexual response in a mammal comprising administering the peptide; or, a pharmaceutical composition comprising a peptide, wherein the peptide is a free acid or pharmaceutically acceptable salt thereof comprising a sequence of His-Phe-Arg-Trp, His-D-Phe-Arg-Trp, a specific homolog of His-Phe-Arg-Trp or a specific homolog of His-D-Phe-Arg-Trp as indicated in the prior art, does not reasonably provide enablement for a pharmaceutical composition comprising a peptide, wherein the peptide is a free acid or pharmaceutically acceptable salt thereof comprising a sequence of His-Phe-Arg-Trp, His-D-Phe-Arg-Trp, a homolog of His-Phe-Arg-Trp or a homolog of His-D-Phe-Arg-Trp, or a method of stimulating sexual response in a mammal by administering the peptide, where the amino acid sequence of the peptide is not defined. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 8-10, 20-22 and 24-27 encompass a pharmaceutical composition comprising a peptide, wherein the peptide is a free acid or pharmaceutically acceptable salt thereof comprising a sequence of His-Phe-Arg-Trp, His-D-Phe-Arg-Trp, a homolog of His-Phe-Arg-Trp or a homolog of His-D-Phe-Arg-Trp (claims 8-10), or a method of stimulating sexual response in a mammal by administering the peptide (claims 20-22 and 24-27). The specification, however, only discloses cursory conclusions without data supporting the findings, which state that the present invention provides a pharmaceutical composition comprising a peptide, which is a free acid or pharmaceutically acceptable salt thereof, comprising a sequence of His-Phe-Arg-Trp, His-D-Phe-Arg-Trp, a homolog of His-Phe-Arg-Trp or a homolog of His-D-Phe-Arg-Trp, which is a melanocortin receptor-specific pharmaceutical and may be used for treatment of sexual dysfunction in a mammal (pages 5-7). There are no indicia that the present application enables the full scope in view of a method of stimulating sexual response in a mammal using the claimed pharmaceutical composition as discussed in the stated rejection. The present application provides no indicia and no teaching/guidance as to how the full scope of the claims is enabled. The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breath of the claims, the absence of working examples, the state of the prior art and relative skill of those in the art, the unpredictability of the art, the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breath of the claims:

The breath of the claims is broad and encompasses unspecified variants regarding the peptides comprising a sequence of His-Phe-Arg-Trp, His-D-Phe-Arg-Trp, a homolog of His-Phe-Arg-Trp or a homolog of His-D-Phe-Arg-Trp, and the treating conditions for stimulating sexual response using the peptides, which are not adequately described or demonstrated in the specification.

(2). The absence or presence of working examples:

There are no working examples indicating the claimed methods in association with the variants except for stimulating sexual response in mammals using compound 1 (Examples 1-17).

(3). The state of the prior art and relative skill of those in the art:

The prior art (references cited at pages 2-4) indicates melanocortin receptor-specific compounds have been used for treatment of sexual dysfunction, e.g., a cyclic α-melanocyte-stimulating hormone (α-MSH) analog, named Melanotan-II (Ac-Nle-cyclo(-Asp-His-D-Phe-Arg-Trp-Lys)-NH_2) or related melanocortin peptides, and the minimum peptide fragment of α-MSH for erectile response is the central tetrapeptide sequence of His-Phe-Arg-Trp, although the mechanism of His-Phe-Arg-Trp induction of erectile response has not been fully elucidated, it has been hypothesized that it involves the central nervous system, probably binding to melanocortin receptor MC3-R and/or MC4-R. However, the general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide teachings on the identities and the effects of the peptides in the treatment, and the treating conditions such as the dose for stimulating sexual response to be considered enabling for variants.

(4). Predictability or unpredictability of the art:

The claims encompass a pharmaceutical composition comprising a peptide comprising a sequence of His-Phe-Arg-Trp, His-D-Phe-Arg-Trp, a homolog of His-Phe-Arg-Trp or a homolog of His-D-Phe-Arg-Trp, which is a free acid, or a method of stimulating sexual response in a mammal by administering the peptide, however, the treating conditions for various peptides or their homologs and the in vivo effects of these peptides are not adequately described in the specification, the invention is highly unpredictable regarding the outcome of the treatment.

(5). The amount of direction or guidance presented and the quantity of experimentation necessary:

The claims are directed to a pharmaceutical composition comprising a peptide comprising a sequence of His-Phe-Arg-Trp, His-D-Phe-Arg-Trp, a homolog of His-Phe-Arg-Trp or a homolog of His-D-Phe-Arg-Trp, which is a free acid, or a method of stimulating sexual response in a mammal by administering the peptide. The specification indicates the binding of compound 1 and Melanotan-II to melanocortin receptors, the agonist activity of compound 1 and using compound 1 to stimulate sexual response in animal models (Examples 2-17). However, the specification has not demonstrated using any other peptide comprising His-Phe-Arg-Trp, His-D-Phe-Arg-Trp or its homolog in a specific dose range to stimulate sexual response in animal models except for the use of compound 1 in the treatment. Moreover, there are no working examples indicating the treating conditions such as dosage for stimulating sexual response in mammals and the effects of these peptides in the treatment. Since the specification fails to provide sufficient teachings on identities of various peptides comprising His-Phe-Arg-Trp, His-D-Phe-Arg-Trp or its homologs, and the treating conditions for stimulating sexual response in mammals, and the in vivo effects of these peptides, it is necessary to have additional

guidance and to carry out further experimentation to assess the effects of various peptides comprising His-Phe-Arg-Trp, His-D-Phe-Arg-Trp or its homologs in the claimed method.

(6). Nature of the Invention

The scope of the claims encompasses a pharmaceutical composition comprising His-Phe-Arg-Trp, His-D-Phe-Arg-Trp, or its a homolog, and a method of stimulating sexual response using the peptide, but the specification does not demonstrate using various peptides in the claimed method. Thus, the disclosure is not enabling for the reasons discussed above.

In summary, the scope of the claim is broader than the enabling disclosure. The working examples do not demonstrate the claimed methods, the outcome of the treatment is unpredictable, and the teaching in the specification is limited, therefore, it is necessary to have additional guidance and to carry out further experimentation to assess the effects of various peptides comprising His-Phe-Arg-Trp, His-D-Phe-Arg-Trp or its homologs in the method of stimulating sexual response in mammals.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 12-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 12-27 are indefinite because the claims lack an essential step in the method of stimulating sexual response in a mammal by administering a pharmaceutical composition. The omitted step is the outcome of method. Claims 13-19 and 21-27 are included in this rejection for

being dependent on a rejected claim and not correcting the deficiency of the claim from which they depend.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 8-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Hruby *et al.* (U. S. Patent 4,649,191).

Hruby *et al.* teach analogs of α-melanotropin such as cyclo(Cys-Glu-His-Phe-D-Lys-Trp-Cys)-OH and cyclo(Cys-Glu-His-Phe-D-Arg-Trp-Cys)-OH exhibit reactivity for central nervous system receptor and can be prepared with water and administered intraperitoneally for in vivo testing (column 1, lines 7-15; columns 4 and 6; Example VI). These cyclic peptides which contain homologs of His-Phe-Arg-Trp and are free acids, can be used to induce a variety of physiological effects such as stimulating sexual activity (column 2, lines 51-65; claims 8-10).

9. Claims 8 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by De Wied *et al.* (U. S. Patent 3,862,928).

De Wied *et al.* teach a peptide of the formula X-L-Met-A-L-His-D-Phe-B-L-Trp-OH, where A is L-Glu or L-Gln, B is L-Arg or L-Lys, and X is Hydrogen, L-Ser or Gly, or a pharmaceutically acceptable salt has psychopharmacological activities and can be prepared in an injection formulation or with suitable auxiliaries in an oral formulation (column 1, lines 29-50; column 4, lines 4-12; Example VI; claims 8 and 10). The term "stimulating sexual response in a

mammal" is an intended use, which does not play weight in the claimed pharmaceutical composition.

10. Claims 8 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Greven *et al.* (U. S. Patent 3,853,836).

De Wied *et al.* teach a peptide of the formula A-L-Glu-L-His-X, where A can be H-D-Met, H-L-Met, or H_2N-B-CO (B is alkylene with 1-6 carbon) and X can be L-Phe-L-Arg-Trp-OH or L-Phe-L-Arg-Trp-Gly-OH, or a pharmaceutically acceptable salt has psychopharmacological activities and can be prepared with a suitable liquid in an injection formulation or with suitable auxiliaries in an oral formulation (column 2, line 58-column 3, line 25; column 5, lines 35-55; Table in columns 6 and 7; claims 8 and 10). The term "stimulating sexual response in a mammal" is an intended use, which does not play weight in the claimed pharmaceutical composition.

Conclusion

11. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (703) 308-9437. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, Ph. D. can be reached on (703) 308-2923. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Chih-Min Kam, Ph. D. CMK
Patent Examiner

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September 20, 2003

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